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=> d que
L4        35346 SEA FILE=CAPLUS ABB=ON  PLU=ON  TUMOR NECROSIS FACTORS/CT
L5              STR
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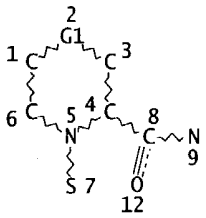

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VAR G1=S/O/N
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  10

STEREO ATTRIBUTES: NONE
L7         1546 SEA FILE=REGISTRY SSS FUL L5
L8          149 SEA FILE=CAPLUS ABB=ON  PLU=ON  L7
L9           13 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 AND L4
L10       23345 SEA FILE=CAPLUS ABB=ON  PLU=ON  METALLOPROT?
L11          79 SEA FILE=CAPLUS ABB=ON  PLU=ON  L10 AND L8
L12          18 SEA FILE=CAPLUS ABB=ON  PLU=ON  L11 AND (TNF OR TACE)
L13          21 SEA FILE=CAPLUS ABB=ON  PLU=ON  L9 OR L12


=> d bib abs hitrn 1-21

L13  ANSWER 1 OF 21  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2004:292580  CAPLUS
DN   141:17177
TI   Identification and characterization of 4-[[4-(2-
     butynyloxy)phenyl]sulfonyl]-N-hydroxy-2,2-dimethyl-(3S)-
     thiomorpholinecarboxamide (TMI-1), a novel dual tumor necrosis
     factor-.alpha.-converting enzyme/matrix metalloprotease
     inhibitor for the treatment of rheumatoid arthritis
AU   Zhang, Yuhua; Xu, Jun; Levin, Jeremy; Hegen, Martin; Li, Guangde;
     Robertshaw, Heidi; Brennan, Fionula; Cummons, Terri; Clarke, Dave;
     Vansell, Nichole; Nickerson-Nutter, Cheryl; Barone, Dauphine; Mohler, Ken;
     Black, Roy; Skotnicki, Jerry; Gibbons, Jay; Feldmann, Marc; Frost, Philip;
     Larsen, Glenn; Lin, Lih-Ling
CS   Wyeth Research, Cambridge, MA, USA
SO   Journal of Pharmacology and Experimental Therapeutics (2004), 309(1),
     348-355
     CODEN: JPETAB; ISSN: 0022-3565
PB   American Society for Pharmacology and Experimental Therapeutics
DT   Journal
LA   English
AB   Tumor necrosis factor (TNF)-.alpha. is a well validated
     therapeutic target for the treatment of rheumatoid arthritis.  TNF
     -.alpha. is initially synthesized as a 26-kDa membrane-bound form (pro-
     TNF) that is cleaved by a Zn-metalloprotease named
     TNF-.alpha.-converting enzyme (TACE) to generate the
     17-kDa, sol., mature TNF-.alpha..  TACE inhibitors
     that prevent the secretion of sol. TNF-.alpha. may be effective
     in treating rheumatoid arthritis (RA) patients.  Using a structure-based
     design approach, we have identified a novel dual TACE/matrix
     metalloprotease (MMP) inhibitor 4-[[4-(2-
     butynyloxy)phenyl]sulfonyl]-N-hydroxy-2,2-dimethyl-(3S)-
     thiomorpholinecarboxamide (TMI-1).  This mol. inhibits TACE and
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several MMPs with nanomolar IC50 values in vitro. In cell-based assays such as monocyte cell lines, human primary monocytes, and human whole blood, it inhibits lipopolysaccharide (LPS)-induced TNF-.alpha. secretion at submicromolar concns., whereas there is no effect on the TNF-.alpha. mRNA level as judged by RNase protection assay. The inhibition of LPS-induced TNF-.alpha. secretion is selective because TMI-1 has no effect on the secretion of other proinflammatory cytokines such as interleukin (IL)-1.beta., IL-6, and IL-8. Importantly, TMI-1 potently inhibits TNF-.alpha. secretion by human synovium tissue explants of RA patients. In vivo, TMI-1 is highly effective in reducing clin. severity scores in mouse prophylactic collagen-induced arthritis (CIA) at 5, 10, and 20 mg/kg p.o. b.i.d. and therapeutic CIA model at 100 mg/kg p.o. b.i.d. In summary, TMI-1, a dual TACE /MMP inhibitor, represents a unique class of orally bioavailable small mol. TNF inhibitors that may be effective and beneficial for treating RA.

IT **287403-39-8**, TMI 1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TMI-1, a novel dual tumor necrosis factor-.alpha.-converting enzyme/matrix **metalloprotease** inhibitor for the rheumatoid arthritis)

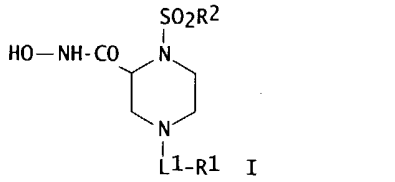
RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:1006921 CAPLUS
DN 140:42210
TI Preparation of 1-sulfonyl-2-piperazinehydroxamic acids as selective inhibitors of human ADAM-10 for treating cancer, arthritis and diseases related to angiogenesis
IN Bannen, Lynne Canne; Co, Erick W.; Jammalamadaka, Vasu; Nuss, John M.; Kim, Moon Hwan; Le Tra, Donna; Lew, Amy; Mac, Morrison B.; Mamo, Shumeye; Wen, Zhaoyang; Xu, Wei
PA Exelixis, Inc., USA
SO PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

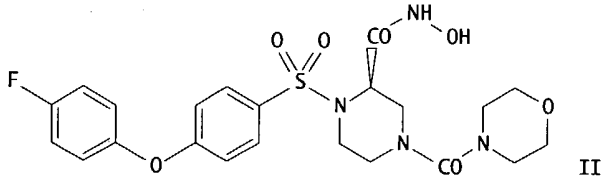
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003106381	A2	20031224	WO 2003-US18262	20030611
	WO 2003106381	A3	20040415		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-388326P P 20020612
OS MARPAT 140:42210
GI



I



II

AB The present invention provides 1-sulfonyl-2-piperazinehydroxamic acids (shown as I; variables defined below; e.g. II) useful for inhibiting the ADAM-10 protein, with selectivity vs. MMP-1. Inhibition activities of 66 examples of I towards .ltoreq.8 **metalloproteinases** are tabulated. Such compds. are useful in the in vitro study of the role of ADAM-10 (and its inhibition) in biol. processes. The present invention also comprises pharmaceutical compns. comprising .gtoreq.1 ADAM-10 inhibitors according to the invention in combination with a pharmaceutically acceptable carrier. Such compns. are useful for the treatment of cancer, arthritis, and diseases related to angiogenesis. Correspondingly, the invention also comprises methods of treating forms of cancer, arthritis, and diseases related to angiogenesis in which ADAM-10 plays a crit. role. A method of prepn. of sulfonyl halide intermediates is claimed. For example, [4-(4-fluorophenoxy)-3,5-difluorophenyl]sulfonyl chloride was prepd. in 3 steps (105, 98 and 83 % yields) starting from 3,4,5-trifluoronitrobenzene, 4-fluorophenol, and Cs2CO3 in DMF and involving intermediates 4-(4-fluorophenoxy)-3,5-difluoronitrobenzene and 4-(4-fluorophenoxy)-3,5-difluoroaniline. The prepd. [4-(4-fluorophenoxy)-3,5-difluorophenyl]sulfonyl chloride was used in a 5-step procedure (65, 78, -, 69 and 62 % yields) to give II involving intermediates (R)-1-[[4-(4-fluorophenoxy)-3,5-difluorophenyl]sulfonyl]-4-boc-piperazine-2-carboxylic acid, Me (R)-1-[[4-(4-fluorophenoxy)-3,5-difluorophenyl]sulfonyl]-4-boc-piperazine-2-carboxylate, Me (R)-1-[[4-(4-fluorophenoxy)-3,5-difluorophenyl]sulfonyl]piperazine-2-carboxylate trifluoroacetate and Me (R)-1-[[4-(4-fluorophenoxy)-3,5-difluorophenyl]sulfonyl]-4-(ethoxycarbonyl)piperazine-2-carboxylate. Although the methods of prepn. of I are not claimed, several example prepns. and characterization data for 66 examples of I are included. For I: L1 is -C(O)-, -S(O)2-, or -(CH2)n-; R1 is -H, -OR11, -(CH2)nR11, -C(O)R11, or -NR12R13; R2 is -R21-L2-R22 (R21 is satd. or mono- or poly-unsatd. C5-C14-mono- or fused poly- cyclic hydrocarbyl, optionally contg. one or two annular heteroatoms per ring and (un)substituted with 1-3 R50 substituents; L2 is -O-, -C(O)-, -CH2-, -NH-, -SO2- or a direct bond; R22 is satd. or mono- or poly- unsatd. C5-C14-mono- or fused polycyclic hydrocarbyl, optionally contg. one or two annular heteroatoms per ring and (un)substituted with 1-3 R50 substituents); n = 0-3; provided that an O or S is not singly bonded to another O or S in a chain of atoms; addnl. details are given in the claims.

IT **637026-58-5P 637026-59-6P 637026-60-9P**
637026-61-0P 637026-62-1P 637026-63-2P
637026-64-3P 637026-65-4P 637026-66-5P
637026-67-6P 637026-68-7P 637026-69-8P
637026-70-1P 637026-71-2P 637026-72-3P
637026-73-4P 637026-74-5P 637026-75-6P
637026-76-7P 637026-77-8P 637026-78-9P
637026-79-0P 637026-80-3P 637026-81-4P
637026-82-5P 637026-83-6P 637026-84-7P
637026-85-8P 637026-86-9P 637026-87-0P

637026-88-1P 637026-89-2P 637026-90-5P
637026-91-6P 637026-92-7P 637026-93-8P
637026-94-9P 637026-95-0P 637026-96-1P
637026-97-2P 637026-98-3P 637026-99-4P
637027-00-0P 637027-01-1P 637027-02-2P
637027-03-3P 637027-04-4P 637027-05-5P
637027-06-6P 637027-07-7P 637027-08-8P
637027-09-9P 637027-10-2P 637027-11-3P
637027-12-4P 637027-13-5P 637027-14-6P
637027-15-7P 637027-16-8P 637027-17-9P
637027-18-0P 637027-19-1P 637027-20-4P
637027-21-5P 637027-22-6P 637027-23-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of 1-sulfonyl-2-piperazinehydroxamic acids as selective inhibitors of human ADAM-10 for treating cancer, arthritis and diseases related to angiogenesis)

L13 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:841815 CAPLUS
DN 140:87055
TI Design and synthesis of orally active inhibitors of TNF synthesis as anti-rheumatoid arthritis drugs
AU Chen, Jian Jeffrey; Dewdney, Nolan; Lin, Xiaohong; Martin, Robert L.; Walker, Keith A. M.; Huang, Jane; Chu, Frances; Eugui, Elsie; Mirkovich, Anna; Kim, Yong; Sarma, Keshab; Arzeno, Humberto; Van Wart, Harold E.
CS Roche Bioscience, Palo Alto, CA, 94304, USA
SO Bioorganic & Medicinal Chemistry Letters (2003), 13(22), 3951-3954
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science B.V.
DT Journal
LA English
OS CASREACT 140:87055
AB A novel series of TNF inhibitors was identified based on the screening of existing MMP inhibitor libraries. Further SAR optimization led to the discovery of a novel lead compd. Its synthesis, efficacy in exptl. animal models, and pharmacokinetic data are discussed.
IT **210916-71-5P**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(design and synthesis of orally active inhibitors of TNF synthesis as anti-rheumatoid arthritis drugs)
IT **210917-20-7P 210917-21-8P 642466-66-8P**
642466-69-1P 642466-71-5P 642466-74-8P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(design and synthesis of orally active inhibitors of TNF synthesis as anti-rheumatoid arthritis drugs)
RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:719248 CAPLUS
DN 139:244721
TI Cytokine inhibitors for use in healing of wounds
IN Olmarker, Kjell
PA Pharmasurgics AB, Swed.; Orthopaedic Research and Development in Gothe
SO PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 2003073981 A2 20030912 WO 2003-SE347 20030304
WO 2003073981 A3 20031127
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2003176332 A1 20030918 US 2002-92919 20020308
PRAI SE 2002-667 A 20020305
US 2002-92919 A 20020308
AB The author discloses the use of inhibitors a pro-inflammatory cytokine, such as **TNF** or IL-1, for improving wound healing. In one example, the administration of infliximab following laminectomy of the sacral vertebrae was shown to limit scaring and adhesion formation.
IT **192329-42-3**, Prinomastat
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(for treatment of wound healing)

L13 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:356407 CAPLUS
DN 138:354243
TI Preparation of amino acid hydroxamic acid allenic arylsulfonamide derivatives as matrix **metalloproteinase** and TACE inhibitors
IN Sandanayaka, Vincent Premaratna; Delos Santos, Efren Guillermo
PA Wyeth Holdings Corporation, USA
SO PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003037852	A1	20030508	WO 2002-US34904	20021031
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1440057	A1	20040728	EP 2002-780545	20021031
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 2003130238	A1	20030710	US 2002-285940	20021101
PRAI US 2001-336050P	P	20011101		
WO 2002-US34904	W	20021031		

OS MARPAT 138:354243
AB Amino acid hydroxamic acid derivs. R6R7C:C:CHCR4R5-Z-Y-X-NR3CR1R2CONOH [X is S, SO, SO2 or P(O)R8, where R8 is (cyclo)alkyl or (hetero)aryl; Y is (hetero)aryl, with the proviso that X and Z may not be bonded to adjacent atoms of Y; Z is O, NH, CH2 or S; R1 is H, (hetero)aryl, cycloheteroalkyl or alk(en)(yn)yl; R2 is any group given for R1 or cycloalkyl; R3 is H, alk(en)(yn)yl or cycloalkyl; R4, R5 are H or alkyl; R6, R7 are H, (cyclo)alkyl, (hetero)aryl or cycloheteroalkyl; or R1/R2, R1/R3 and R6/R7 may form rings] were prepd. for treating disease conditions mediated by **TNF**-.alpha.. Thus, p-CH2:C:CHCH2OC6H4SO2-DL-Val-NHOH was prepd. via sulfonylation of DL-Val-OMe.HCl with p-CH2:C:CHCH2OC6H4SO2Cl (prepn.

given) and assayed for in vitro inhibition of matrix **metalloproteinase** (MMP) and **TACE** (IC50 = 2,668, 36, 21, and 51 nM for MMP-1, MMP-9, MMP-13 and **TACE**, resp.).

IT **519056-07-6P 519056-10-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of amino acid hydroxamic acid allenic arylsulfonamide derivs. as matrix **metalloproteinase** and **TACE** inhibitors)

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:249856 CAPLUS
DN 140:104428
TI Identification of a Selectivity Determinant for Inhibition of Tumor Necrosis Factor-.alpha. Converting Enzyme by Comparative Modeling
AU Wasserman, Zelda R.; Duan, James J.-W.; Voss, Matthew E.; Xue, Chu-Biao; Cherney, Robert J.; Nelson, David J.; Hardman, Karl D.; Decicco, Carl P.
CS Structural Biology and Molecular Design Group, Bristol-Myers Squibb Company, Wilmington, DE, 19880, USA
SO Chemistry & Biology (2003), 10(3), 215-223
CODEN: CBOLE2; ISSN: 1074-5521
PB Cell Press
DT Journal
LA English
AB Inhibition of tumor necrosis factor-.alpha. converting enzyme (**TACE**) is a widespread objective in the search for disease modifying agents to combat rheumatoid arthritis and other autoimmune diseases. Until recently, most of the inhibitors in the literature have shown concomitant activity against the related matrix **metalloproteinases** (MMPs), producing undesired side effects. Here we describe the successful search for a **TACE** selectivity mechanism. We built a homol. model based on the crystal structure of the related snake venom protein atrolysin. Comparison of the model with crystal structures of MMPs suggested a uniquely shaped S1' pocket that might be exploited for selectivity. A novel .gamma.-lactam scaffold was used to explore the activity profile of P1' sidechains, resulting in highly selective compds. consistent with this hypothesis. Transferability of the hypothesis was then demonstrated with five other distinct scaffolds.

IT **192329-42-3 250581-11-4 250581-20-5 642487-21-6**
RL: PAC (Pharmacological activity); BIOL (Biological study)
(identification of a selectivity determinant for inhibition of tumor necrosis factor-.alpha. converting enzyme by comparative modeling)

RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:813910 CAPLUS
DN 137:304778
TI Method using **TNF**-.alpha. converting enzyme (**TACE**) inhibitors and EGF receptor kinase inhibitors for the treatment of polycystic kidney disease
IN Frost, Philip; Levin, Jeremy Ian
PA American Dyanamid Company, USA
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002083112	A2	20021024	WO 2002-US10751	20020405
	WO 2002083112	A3	20030925		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CH, CN, CO,

CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM,
HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

BR	2002008784	A	20040622	BR 2002-8784	20020405
US	2004063672	A1	20040401	US 2003-473857	20031002
PRAI US	2001-283087P	P	20010411		
	WO 2002-US10751	W	20020405		

OS MARPAT 137:304778

AB The invention provides a method for treating, inhibiting the progression of, or eradicating polycystic kidney disease in a patient in need thereof which comprises providing an effective amt. of a **TACE** inhibitor compd., alone or in combination with an effective amt. of an EGF receptor kinase inhibitor.

IT **287403-55-8 287405-51-0**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**TNF**-.alpha. converting enzyme (**TACE**) inhibitors and EGF receptor kinase inhibitors for treatment of polycystic kidney disease)

IT **287409-04-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**TNF**-.alpha. converting enzyme (**TACE**) ste inhibitors and EGF receptor kinase inhibitors for treatment of polycystic kidney disease)

L13 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:793396 CAPLUS
DN 137:289028
TI Use of **TNF** inhibitor for treatment of whiplash associated disorder
IN Olmarker, Kjell; Rydevik, Bjoern
PA A+ Science Invest AB, Swed.
SO PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002080892	A1	20021017	WO 2002-SE672	20020405

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI SE 2001-1257 A 20010406

AB The use of a tumor necrosis factor (**TNF**) inhibitor for the prodn. of a pharmaceutical compn. for treatment of whiplash assocd. disorder (WAD) is disclosed. Also a method for treatment of whiplash assocd. disorder (WAD) is disclosed. The inhibitor can be a specific **TNF** blocking substance (antibody, receptor antagonist, antisense oligonucleotide) or a non-specific **TNF** blocking substance (MMP inhibitor, quinolone, thalidomide, etc.).

IT **192329-42-3**, Prinomastat
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological

study); USES (Uses)
(use of TNF inhibitor for treatment and diagnosis of whiplash assocd. disorder)
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:793395 CAPLUS
DN 137:304790
TI Use of a TNF inhibitor for the treatment of low back pain
IN Olmarker, Kjell; Rydevik, Bjoern
PA A+ Science Invest AB, Swed.
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002080891	A1	20021017	WO 2002-SE671	20020405

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI SE 2001-1256 A 20010406
AB The use of a tumor necrosis factor (TNF) inhibitor for the prodn. of a pharmaceutical compn. for treatment of low back pain and in particular of low back pain due to local irritation of annulus-related nerve fibers by disk derived substances is described. Also a method for treatment of low back pain is disclosed. For example, a patient was given infliximab, a selective monoclonal antibody that inhibits only TNF, at 5 mg/kg for treatment of low back pain. Approx. 1.5 h after completing the administration the patient started to feel symptoms of relief regarding his pain. The improvement was found to be dramatic at the follow-up examns. and persisted during 4 wk.
IT **192329-42-3**, Prinomastat
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of TNF inhibitors for treatment of low back pain)
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:417356 CAPLUS
DN 137:212725
TI The C-terminal domains of **TACE** weaken the inhibitory action of N-TIMP-3
AU Lee, Meng-Huee; Verma, Vandana; Maskos, Klaus; Becherer, J. David; Knauper, Vera; Dodds, Philippa; Amour, Augustin; Murphy, Gillian
CS School of Biological Sciences, University of East Anglia, Norwich, NR4 7TJ, UK
SO FEBS Letters (2002), 520(1-3), 102-106
CODEN: FEBLAL; ISSN: 0014-5793
PB Elsevier Science B.V.
DT Journal
LA English
AB Tumor necrosis factor-.alpha. converting enzyme (**TACE**) is an ADAM (a disintegrin and **metalloproteinases**) that comprises an active catalytic domain and several C-terminal domains. We compare the binding affinity and assocn. rate consts. of the N-terminal domain form of wild-type tissue inhibitor of **metalloproteinase** (TIMP-3; N-TIMP-3) and its mutants against full-length recombinant **TACE**

and the truncated form of its catalytic domain. We show that the C-terminal domains of TACE substantially weaken the inhibitory action of N-TIMP-3. Further probing with hydroxamate inhibitors indicates that both forms of TACE have similar active site configurations. Our findings highlight the potential role of the C-terminal domains of ADAM proteinases in influencing TIMP interactions.

IT **192329-42-3**, AG3340
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(activity of hydroxamate inhibitors toward mutant forms of TACE indicates C-terminal domains of TACE have little effect on active site configuration)

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:312012 CAPLUS
DN 136:340996
TI Preparation of sulfamides as **metalloprotease** inhibitors
IN Broka, Chris Allen; Campbell, Jeffrey Allen; Castelhano, Arlindo Lucas; Chen, Jian Jeffrey; Hendricks, Robert Than; Melnick, Michael Joseph; Walker, Keith Adrian Murray
PA Syntex (U.S.A.) LLC, USA; Agouron Pharmaceuticals, Inc.
SO U.S., 47 pp., Cont.-in-part of U.S. 6,143,744.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6376506	B1	20020423	US 1999-469677	19991222
	CA 2278694	AA	19980730	CA 1998-2278694	19980114
	AU 9866140	A1	19980818	AU 1998-66140	19980114
	AU 730127	B2	20010222		
	EP 958287	A1	19991124	EP 1998-907943	19980114
	EP 958287	B1	20020911		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	BR 9807508	A	20000321	BR 1998-7508	19980114
	NZ 336625	A	20010427	NZ 1998-336625	19980114
	JP 2001523222	T2	20011120	JP 1998-531537	19980114
	JP 3563411	B2	20040908		
	AT 223909	E	20020915	AT 1998-907943	19980114
	ZA 9800376	A	19980723	ZA 1998-376	19980116
	US 5998412	A	19991207	US 1998-9951	19980121
	NO 9903587	A	19990922	NO 1999-3587	19990722
	MX 9906822	A	20000131	MX 1999-6822	19990722
	US 6130220	A	20001010	US 1999-369677	19990805
	US 6143744	A	20001107	US 1999-369501	19990805
PRAI	US 1997-36714P	P	19970123		
	US 1997-62209P	P	19971016		
	US 1998-9951	A3	19980121		
	US 1999-369501	A2	19990805		
	WO 1998-EP180	W	19980114		

OS MARPAT 136:340996
AB Sulfamides RCOCR1R2NR3SO2NR4R5 [R = OH, NHOH or N/O-alkyl or -aryl derivs.; R1, R2, R3 = H, alkyl, alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl,(hetero)aryl, acylalkyl, etc.; R1R2C may be a (hetero)carbocycle or R3 together with R1 or R2 form a heterocycloamino group; R4, R5 = H, alkyl, heteroalkyl, cycloalkyl, cycloalkylalkyl, aryl, (hetero)aralkyl or -aralkenyl; R4R5N may be a heterocycloamino group or R4 or R5 together with R3 forms an alkylene group (with provisos)], as individual isomers or mixts. of isomers, or their pharmaceutically-acceptable salts or prodrugs were prepd. as inhibitors of **metalloproteases**. Thus, 2-(R)-[(1,2,3,4-tetrahydro-.beta.-carbolino-2-sulfonyl)amino]propionic acid (claimed compd.) was prepd. by treating D-alanine Me ester hydrochloride with chlorosulfonyl isocyanate/2-chloroethanol, reaction of the oxazolidone formed with

1,2,3,4-tetrahydro-.beta.-carboline, and sapon. **Metalloprotease** and TNF-.alpha. inhibitory test data are tabulated.

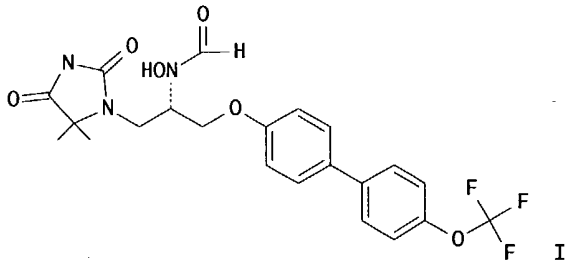
IT **210916-51-1P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of sulfamides as **metalloprotease** inhibitors)

IT **210915-28-9P 210915-31-4P 210915-34-7P**
210915-35-8P 210915-37-0P 210915-39-2P
210915-42-7P 210915-43-8P 210915-44-9P
210915-45-0P 210915-46-1P 210915-47-2P
210915-49-4P 210915-50-7P 210915-51-8P
210915-52-9P 210915-54-1P 210915-59-6P
210915-60-9P 210915-61-0P 210915-62-1P
210915-67-6P 210915-68-7P 210915-74-5P
210915-82-5P 210915-86-9P 210915-87-0P
210915-88-1P 210915-89-2P 210915-90-5P
210915-92-7P 210915-93-8P 210915-94-9P
210915-95-0P 210915-96-1P 210915-97-2P
210915-99-4P 210916-00-0P 210916-01-1P
210916-03-3P 210916-04-4P 210916-05-5P
210916-06-6P 210916-07-7P 210916-09-9P
210916-14-6P 210916-16-8P 210916-17-9P
210916-46-4P 210916-48-6P 210916-49-7P
210916-50-0P 210916-54-4P 210916-62-4P
210916-63-5P 210916-64-6P 210916-65-7P
210916-70-4P 210916-71-5P 210916-73-7P
210916-74-8P 210916-75-9P 210916-77-1P
210916-78-2P 210916-79-3P 210916-80-6P
210917-17-2P 416846-37-2P 416846-38-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of sulfamides as **metalloprotease** inhibitors)

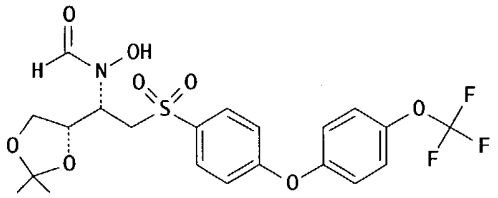
IT **210917-47-8P 210917-52-5P 210917-53-6P**
210917-68-3P 210917-69-4P 210917-72-9P
210917-73-0P 416846-40-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of sulfamides as **metalloprotease** inhibitors)

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:878331 CAPLUS
DN 136:160851
TI Phenoxyphenyl Sulfone N-Formylhydroxylamines (Retrohydroxamates) as Potent, Selective, Orally Bioavailable Matrix **Metalloproteinase** Inhibitors
AU Wada, Carol K.; Holms, James H.; Curtin, Michael L.; Dai, Yujia; Florjancic, Alan S.; Garland, Robert B.; Guo, Yan; Heyman, H. Robin; Stacey, Jamie R.; Steinman, Douglas H.; Albert, Daniel H.; Bouska, Jennifer J.; Elmore, Ildiko N.; Goodfellow, Carole L.; Marcotte, Patrick A.; Tapang, Paul; Morgan, Douglas W.; Michaelides, Michael R.; Davidsen, Steven K.
CS Cancer Research Area, Abbott Laboratories, Abbott Park, IL, 60064-6100, USA
SO Journal of Medicinal Chemistry (2002), 45(1), 219-232
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
GI



I



II

AB 51A novel series of sulfone N-formylhydroxylamines (retrohydroxamates) have been investigated as matrix **metalloproteinases** (MMP) inhibitors. The substitution of the ether linkage of ABT-770 (I) with a sulfone group led to a substantial increase in activity against MMP-9 but was accompanied by a loss of selectivity for inhibition of MMP-2 and -9 over MMP-1 and diminished oral exposure. Replacement of the biphenyl P1' substituent with a phenoxyphenyl group provided compds. that are highly selective for inhibition of MMP-2 and -9 over MMP-1. Optimization of the substituent adjacent to the retrohydroxamate center in this series led to the clin. candidate ABT-518 (II), a highly potent, selective, orally bioavailable MMP inhibitor that has been shown to significantly inhibit tumor growth in animal cancer models.

IT **192329-42-3**, Prinomastat.
RL: PAC (Pharmacological activity); BIOL (Biological study)
(phenoxyphenyl sulfone N-formylhydroxylamines (retrohydroxamates) as potent, selective, orally bioavailable matrix **metalloproteinase** inhibitors)

RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:780015 CAPLUS
DN 136:128574
TI Discovery of selective hydroxamic acid inhibitors of tumor necrosis factor-.alpha. converting enzyme
AU Holms, James; Mast, Katherine; Marcotte, Patrick; Elmore, Ildiko; Li, Junling; Pease, Lori; Glaser, Keith; Morgan, Douglas; Michaelides, Michael; Davidsen, Steven
CS Dept. 47J, Cancer Research Area, Abbott Laboratories, Abbott Park, IL, 60064, USA
SO Bioorganic & Medicinal Chemistry Letters (2001), 11(22), 2907-2910
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
AB Modification of the P1' substituent of macrocyclic matrix **metalloproteinase** (MMP) inhibitors provided compds. that are selective for inhibition of tumor necrosis factor-.alpha. converting enzyme (**TACE**) over MMP-1 and MMP-2. Several analogs potently inhibited the release of TNF-.alpha. in a THP-1 cellular assay. Compds. contg. a trimethoxyphenyl group in the P1' substituent demonstrated **TACE** selectivity across several series of hydroxamate-based inhibitors.
IT **192329-42-3**, Prinomastat **393525-55-8**

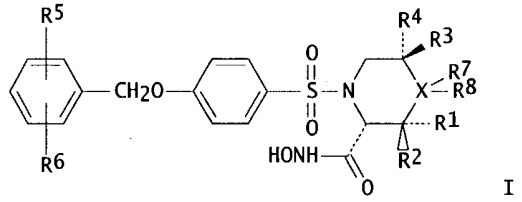
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(discovery of selective hydroxamic acid inhibitors of tumor necrosis factor-.alpha. converting enzyme over inhibition of MMP-1 and MMP-2 in relation to structure and inhibition of TNF-.alpha. release)

RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

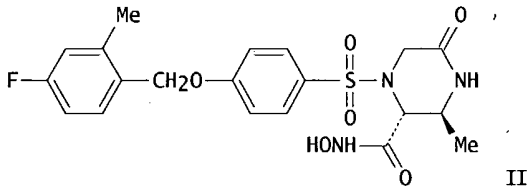
L13 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:167662 CAPLUS
DN 134:207829
TI Preparation of N-(p-benzyloxybenzenesulfonylamino)piperidine and -piperazine derivatives as selective inhibitors of aggrecanase in osteoarthritis treatment
IN Noe, Mark Carl; Letavic, Michael A.; Hawkins, Joel M.
PA Pfizer Products Inc., USA
SO Eur. Pat. Appl., 65 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1081137	A1	20010307	EP 2000-306745	20000808
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	CA 2315481	AA	20010212	CA 2000-2315481	20000810
	JP 2001114765	A2	20010424	JP 2000-243139	20000810
	JP 2003040800	A2	20030213	JP 2002-210977	20000810
	BR 2000003568	A	20010403	BR 2000-3568	20000814
	JP 2004168786	A2	20040617	JP 2004-27695	20040204
PRAI	US 1999-148464P	P	19990812		
	JP 2000-243139	A3	20000810		

OS MARPAT 134:207829
GI



I



II

AB The title compds. (I) or therapeutically acceptable salts thereof [wherein X is carbon or nitrogen; R1 and R2 are independently selected from the group consisting of hydrogen, hydroxy, and Me, wherein at least one of R1 and R2 is methyl; R3 and R4 are independently selected from the group consisting of hydrogen, hydroxy, and Me, or R3 and R4 may be taken together to form a carbonyl group; and R5 and R6 are independent substituents in the ortho, meta, or para positions and are independently selected from the group consisting of hydrogen, halogen, cyano, Me, and ethyl; with the provisos: when X is carbon, then R7 and R8 are both hydrogen and at least one of R1, R2, R3, and R4 is hydroxy; when X is carbon and R5 is para-halo, then at least one of R6, R3, and R4 is not

hydrogen; when X is nitrogen, then R8 is not present and R7 is hydrogen or a group of the formula: wherein, Y is -CH2-NH2 or -NH-CH3; and when X is nitrogen and R7 is H, then R3 and R4 are taken together to form a carbonyl group] (e.g. II) are prepd. A method of treatment for osteoarthritis involves inhibitors of aggrecanase that demonstrate IC50s of less than 20 nM and demonstrate differential potency against matrix **metalloproteinases** (MMPs) and a disintegrin and **metalloproteinases** (ADAMs or reprolysins). These compds. are useful for the treatment of a condition selected from the group consisting of osteoarthritis, joint injury, reactive arthritis, acute pyrophosphate arthritis (pseudogout), psoriatic arthritis, juvenile rheumatoid arthritis, inflammatory bowel disease, Crohn's disease, emphysema, acute respiratory distress syndrome, asthma, chronic obstructive pulmonary disease, Alzheimer's disease, organ transplant toxicity, cachexia, allergic reactions, allergic contact hypersensitivity, cancer, tissue ulceration, restenosis, periodontal disease, epidermolysis bullosa, osteoporosis, loosening of artificial joint implants, atherosclerosis, aortic aneurysm, congestive heart failure, myocardial infarction, stroke, cerebral ischemia, head trauma, spinal cord injury, neurodegenerative disorders, autoimmune disorders, Huntington's disease, Parkinson's disease, migraine, depression, peripheral neuropathy, pain, cerebral amyloid angiopathy, nootropic or cognition enhancement amyotrophic lateral sclerosis, multiple sclerosis, ocular angiogenesis, corneal injury, muscular degeneration, abnormal wound healing, burns, diabetes, corneal scarring, scleritis, AIDS, or sepsis or septic shock, in a mammal. II showed IC50 of <10, 10< to <20, >1,000, and <10 .mu.M against aggrecanase, MMP-13, MMP-1, and **TACE**, resp.

IT **329040-88-2P 329040-89-3P 329040-90-6P**
329040-93-9P 329040-97-3P 329041-10-3P
329041-47-6P 329041-48-7P 329041-50-1P
329041-51-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-(p-benzyloxybenzenesulfonylamino)piperidine and -piperazine derivs. as selective inhibitors of aggrecanase in osteoarthritis treatment)

IT **329041-49-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; prepn. of N-(p-benzyloxybenzenesulfonylamino)piperidine and -piperazine derivs. as selective inhibitors of aggrecanase in osteoarthritis treatment)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:833554 CAPLUS
DN 134:4950
TI Preparation of 1-phenylsulfonylazine-2-hydroxamates as **metalloproteinase** inhibitors
IDS
IN Zook, Scott E.; Dagnino, Raymond, Jr.; Deason, Michael E.; Bender, Steven L.; Melnick, Michael J.
PA Agouron Pharmaceuticals, Inc., USA
SO U.S., 45 pp., Cont.-in-part of U.S. 5,753,653.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 6153757	A	20001128	US 1998-11971	19980629
WO 9720824	A1	19970612	WO 1996-US19328	19961205

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

	US 5753653	A	19980519	US 1996-759713	19961206
	US 6500948	B1	20021231	US 2000-675555	20000929
	US 2003130506	A1	20030710	US 2002-298842	20021118
PRAI	US 1995-41496P	P	19951208		
	WO 1996-US19328	W	19961205		
	US 1996-759713	A2	19961206		
	US 1995-569766	A2	19951208		
	US 1998-11971	A3	19980629		
	US 2000-675555	A3	20000929		

OS MARPAT 134:4950

AB RZZ1SO2NR1CHR2CONHOH [I; R = (hetero)aryl; R1R2 = atoms to complete a heterocyclic ring; Z = O or S; Z1 = 1,4-phenylene] were prepd. Thus, (R)-N-hydroxy-1-[4-(4-chlorophenoxy)benzenesulfonyl]-4-(tert-butoxycarbonyl)piperazine-2-carboxamide (m.p. 94.6.degree.), prepd. from (R)-piperazine-2-carboxylic acid in 4 steps, demonstrated 77.6% inhibition of lung metastases in a female mouse Lewis lung carcinoma model at 50 mg/kg (i.p.).

IT **192329-44-5P 192329-52-5P 192329-62-7P**
192329-64-9P 192329-79-6P 192330-51-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of heterocyclic **metalloproteinase**-inhibitor antitumor agents and antiarthritics)

IT **192329-42-3P 192329-43-4P 192329-45-6P**
192329-46-7P 192329-47-8P 192329-48-9P
192329-49-0P 192329-50-3P 192329-51-4P
192329-53-6P 192329-54-7P 192329-56-9P
192329-57-0P 192329-58-1P 192329-59-2P
192329-60-5P 192329-63-8P 192329-65-0P
192329-68-3P 192329-69-4P 192329-70-7P
192329-71-8P 192329-73-0P 192329-74-1P
192329-75-2P 192329-76-3P 192329-77-4P
192329-78-5P 192329-95-6P 192329-98-9P
192330-14-6P 192330-15-7P 192330-16-8P
192330-17-9P 192330-18-0P 192330-19-1P
192330-20-4P 192330-21-5P 192330-22-6P
192330-27-1P 192330-28-2P 192330-33-9P
192330-52-2P 192330-53-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of heterocyclic **metalloproteinase**-inhibitor antitumor agents and antiarthritics)

IT **192330-67-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of heterocyclic **metalloproteinase**-inhibitor antitumor agents and antiarthritics)

IT **192329-97-8P 192329-99-0P 192330-02-2P**
192330-05-5P 192330-10-2P 192330-13-5P
192330-23-7P 192330-26-0P 192330-50-0P
192330-56-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of heterocyclic **metalloproteinase**-inhibitor antitumor agents and antiarthritics)

RE.CNT 124 THERE ARE 124 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:133668 CAPLUS
DN 132:166245
TI Preparation of 4-phenylsulfonyl-3-morpholinehydroxamic acids and analogs

as tumor necrosis factor .alpha.-convertase inhibitors

IN McClure, Kim Francis; Noe, Mark Carl; Letavic, Michael Anthony; Chupak, Louis Stanley

PA Pfizer Products Inc., USA

SO PCT Int. Appl., 87 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000009492	A1	20000224	WO 1999-IB1392	19990805
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2340182	AA	20000224	CA 1999-2340182	19990805
	AU 9949250	A1	20000306	AU 1999-49250	19990805
	BR 9912944	A	20010508	BR 1999-12944	19990805
	EP 1104412	A1	20010606	EP 1999-933079	19990805
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2003526604	T2	20030909	JP 2000-564944	19990805
	US 2003181441	A1	20030925	US 1999-373182	19990812
PRAI	US 1998-96256P	P	19980812		
	WO 1999-IB1392	W	19990805		

instant

OS MARPAT 132:166245

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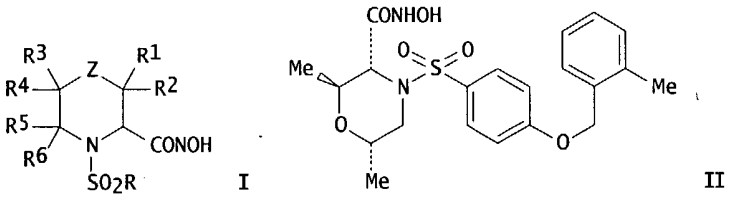

AB Title compds. [I; R = (un)substituted (hetero)aryloxy(hetero)aryl; R1-R6 = H, OH, alkyl, alkoxy, etc.; Z = O, SOO-2, [(un)substituted alkyl]imino] were prepd. Thus, D-threonine was converted in 7 steps to title compd. II. Data for biol. activity of I were given.

IT **259132-45-1P 259132-46-2P 259132-47-3P**
259132-48-4P 259132-49-5P 259132-50-8P
259132-51-9P 259132-52-0P 259132-53-1P
259132-54-2P 259132-55-3P 259132-56-4P
259132-57-5P 259132-58-6P 259132-59-7P
259132-60-0P 259132-61-1P 259132-62-2P
259132-63-3P 259132-64-4P 259132-65-5P
259132-66-6P 259132-67-7P 259132-68-8P
259132-69-9P 259132-70-2P 259132-71-3P
259132-72-4P 259132-73-5P 259132-74-6P
259132-75-7P 259132-76-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 4-phenylsulfonyl-3-morpholinehydroxamic acids and analogs as tumor necrosis factor .alpha.-convertase inhibitors)

IT **259132-86-0P 259132-98-4P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of 4-phenylsulfonyl-3-morpholinehydroxamic acids and analogs as tumor necrosis factor .alpha.-convertase inhibitors)
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:736704 CAPLUS
DN 131:351341
TI Preparation of arylsulfonylheterocyclylhydroxamic acids as **metalloproteinase** and TNF inhibitors for the treatment of inflammatory disorders
IN Voss, Matthew E.; Decicco, Carl P.; Wexler, Ruth R.
PA Du Pont Pharmaceuticals Company, USA
SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9958531	A1	19991118	WO 1999-US10357	19990512
	W: AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2330108	AA	19991118	CA 1999-2330108	19990512
	AU 9939825	A1	19991129	AU 1999-39825	19990512
	EP 1077978	A1	20010228	EP 1999-922940	19990512
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
	BR 9910678	A	20011002	BR 1999-10678	19990512
	JP 2002514647	T2	20020521	JP 2000-548335	19990512
	US 6365587	B1	20020402	US 1999-312066	19990513
	US 2003073682	A1	20030417	US 2002-115231	20020403
PRAI	US 1998-85394P	P	19980514		
	WO 1999-US10357	W	19990512		
	US 1999-312066	A3	19990513		

OS MARPAT 131:351341
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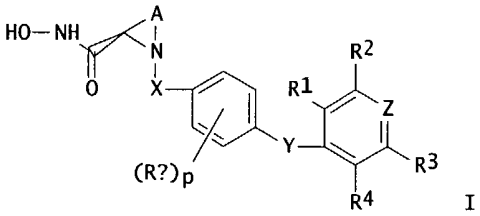

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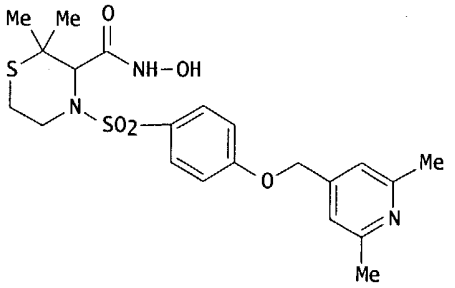

II

AB Title compds. (I) [where ring A = (un)substituted 5-8 membered heterocycle contg. 0-1 addnl. heteroatoms; Rb = independently F or Me; X = CH2, CO, CO2, CONH, SO, SO2, SONH, or SO2NH; Y = (CH2)n; CR5R6O, OCR5R6, S(O)pCH2, CH2S(O)p, CH2NH or NHCH2; Z = CH or N; R1, R2, R3 = halo, (O)Me, (O)Et, (O)Pr-i, or (O)CF3; or R1 = H; R4 = H; or R3 and R4 taken together with C atoms = (un)substituted 5-6 membered (hetero)arom. ring; R5 and R6 = independently H, F, or Me; n = 1-3; p = 0-2] were prepd. as **metalloproteinase** and (tumor necrosis factor) **TNF** inhibitors and are useful for the treatment of inflammatory disorders (no data). For example, (S)-II was prepd. by amidation of 4-HOC6H4SO2Cl with Me 2,2-dimethylthiomorpholine-3(S)-carboxylate (37%), followed by etherification of the phenol with 4-chloromethyl-2,6-dimethylpyridine.HCl (82%), deesterification of the carboxylate, and addn. of HONH2.HCl (33%). Some compds. of the invention are selective for **TNF**-C over matrix **metalloproteinase** inhibition and are expected to produce fewer toxic side effects related to tendonitis and fibroplasia (no data).

IT **250581-57-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of arylsulfonylheterocyclylhydroxamic acids as **metalloproteinase** and **TNF** inhibitors for the treatment of inflammatory disorders)

IT **250581-10-3P 250581-11-4P 250581-19-2P**
250581-20-5P 250581-21-6P 250581-22-7P
250581-23-8P 250581-24-9P 250581-25-0P
250581-26-1P 250581-27-2P 250581-28-3P
250581-30-7P 250581-31-8P 250581-32-9P
250581-33-0P 250581-35-2P 250581-51-2P
250581-52-3P 250581-53-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compd.; prepn. of arylsulfonylheterocyclylhydroxamic acids as **metalloproteinase** and **TNF** inhibitors for the treatment of inflammatory disorders)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:665134 CAPLUS
DN 131:281567
TI Therapeutic agents for myelodysplastic syndrome
IN Arima, Naomichi; Arimura, Mitsuo
PA Kanebo, Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 11286455	A2	19991019	JP 1998-105793	19980331
PRAI	JP 1998-105793		19980331		

AB The agents contain matrix **metalloprotease** inhibitors, **TNF**-.alpha.-converting enzyme inhibitors, and/or Fas ligand solubilization inhibitors as active ingredients. The agents suppress decrease in bone marrow cells due to apoptosis. [4-(N-Hydroxyamino)-2(R)-isobutyl-3(S)-methylsuccinyl]-L-phenylglycine-N-methylamide (I) inhibited apoptosis of nucleated bone marrow cells sampled from myelodysplastic syndrome patients. Pharmaceutical prepns. contg. contg. I, etc., were also given.

IT **192329-42-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(myelodysplastic syndrome treatment with matrix **metalloprotease** inhibitors, **TNF**.alpha.-converting enzyme inhibitors, and/or Fas ligand solubilization inhibitors)

L13 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:550410 CAPLUS
DN 129:175560
TI Preparation of N-arylsulfonylpiperidine-2-hydroxamic acids as matrix **metalloproteinase** and tumor necrosis factor production inhibitors
IN McClure, Kim Francis
PA Pfizer Inc., USA
SO PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DT Patent
LA English

prov 13 8/12

IDS

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9834918	A1	19980813	WO 1998-IB64	19980116
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2280151	AA	19980813	CA 1998-2280151	19980116
	AU 9853366	A1	19980826	AU 1998-53366	19980116
	AU 722784	B2	20000810		
	EP 960098	A1	19991201	EP 1998-900124	19980116
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
	BR 9807678	A	20000215	BR 1998-7678	19980116
	JP 2000510162	T2	20000808	JP 1998-534040	19980116
	NZ 336836	A	20010223	NZ 1998-336836	19980116
	AP 958	A	20010417	AP 1998-1179	19980205
	W: BW, GM, KE, MW, UG, ZM, ZW				
	TW 502020	B	20020911	TW 1998-87101709	19980209
	ZA 9801061	A	19990810	ZA 1998-1061	19980210
	HR 980070	B1	20021031	HR 1998-980070	19980212
	BG 63430	B1	20020131	BG 1999-103641	19990805
	NO 9903836	A	19991008	NO 1999-3836	19990810
	MX 9907385	A	20000731	MX 1999-7385	19990810
	US 6599890	B1	20030729	US 2000-708328	20001108
PRAI	US 1997-37600P	P	19970211		
	WO 1998-IB64	W	19980116		
	US 1998-125055	A1	19980804		

OS MARPAT 129:175560
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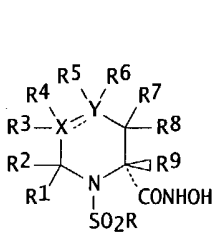

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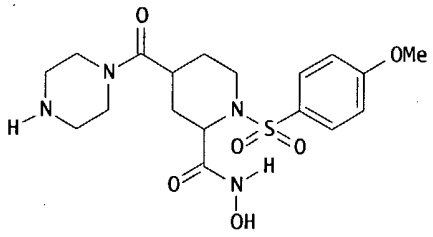


II

AB Title compds. [I; R = alkyl, aryl(oxy), etc.; R1-R9 = H, (un)substituted alkyl, etc.; X = C, O, S (sic); Y = C, O, SO-2, N (sic); dashed line = optional addnl. bond] were prepd. as matrix **metalloproteinase**

and tumor necrosis factor prodn. inhibitors (no data). Thus, (R)-MeO2CCH2CH2CH(NHCO2CH2PH)CO2CMe3 was converted in 10 steps to title compd. (R,R)-II.

IT **211381-13-4P 211381-14-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-arylsulfonylpiperidine-2-hydroxamic acids as matrix **metalloproteinase** and tumor necrosis factor prodn. inhibitors)

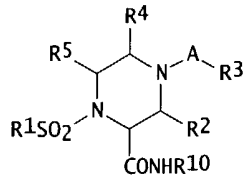
IT **211381-48-5P 211381-50-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of N-arylsulfonylpiperidine-2-hydroxamic acids as matrix **metalloproteinase** and tumor necrosis factor prodn. inhibitors)

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:424232 CAPLUS
DN 129:95510
TI Preparation of 2-piperazinecarboxamides as inhibitors of MMP or **TNF**
IN Neya, Masahiro; Yamazaki, Hitoshi; Kayakiri, Natsuko; Sato, Kentaro; Oku, Teruo
PA Fujisawa Pharmaceutical Co., Ltd., Japan; Neya, Masahiro; Yamazaki, Hitoshi; Kayakiri, Natsuko; Sato, Kentaro; Oku, Teruo
SO PCT Int. Appl., 199 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9827069	A1	19980625	WO 1997-JP4613	19971215
	W: AU, CA, CN, HU, IL, JP, KR, MX, US, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	ZA 9711284	A	19980623	ZA 1997-11284	19971215
	CA 2275478	AA	19980625	CA 1997-2275478	19971215
	AU 9854122	A1	19980715	AU 1998-54122	19971215
	EP 948489	A1	19991013	EP 1997-947944	19971215
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
	JP 2001506257	T2	20010515	JP 1998-527536	19971215
	KR 2000057595	A	20000925	KR 1999-705374	19990615
	US 6333324	B1	20011225	US 1999-319928	19990726
	US 2002128270	A1	20020912	US 2001-982869	20011022
	US 6489324	B2	20021203		
	US 2003060473	A1	20030327	US 2002-262841	20021003
PRAI	AU 1996-4249	A	19961217		
	AU 1997-7156	A	19970603		
	AU 1997-8568	A	19970814		
	WO 1997-JP4613	W	19971215		
	US 1999-319928	A3	19990726		
	US 2001-982869	A3	20011022		

OS MARPAT 129:95510
GI



I

IDS

AB The title compds. [I; A = SO2, C(O); R1 = (un)substituted aryl, heterocyclic, lower alkyl, lower alkenyl; R2 = H, (un)substituted lower alkyl, aryl, heterocyclic; R3 = (un)substituted lower alkyl, lower alkoxy, aryloxy, etc.; R4 = H, (un)substituted lower alkyl, aryl, heterocyclic; R5 = H, (un)substituted lower alkyl, aryl, heterocyclic; R10 = OH, protected OH] and their pharmaceutically acceptable salts, useful for prophylactic and therapeutic treatment of MMP- or TNF.alpha.-mediated diseases, were prepd. Thus, treatment of a soln. of (2R)-1-(4-nitrobenzenesulfonyl)-4-methanesulfonylpiperazine-2-[N-(2-tetrahydropyranyloxy)]carboxamide in MeOH with 10% HCl-MeOH afforded (2R)-I [R1 = 4-O2NC6H4SO2; R2 = R4 = R5 = H; R3 = Me; R10 = OH] which showed 95.3% inhibition of collagenase activity at 1x10-6 M.

IT **209588-53-4P 209588-58-9P 209588-68-1P**
209589-31-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of 2-piperazinecarboxamides as inhibitors of MMP or TNF)

IT **209588-64-7P 209588-73-8P 209588-77-2P**
209588-81-8P 209588-87-4P 209588-93-2P
209588-98-7P 209589-04-8P 209589-10-6P
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209591-58-2P 209591-59-3P 209591-60-6P
209591-61-7P 209591-62-8P 209591-63-9P
209591-64-0P 209591-65-1P 209591-66-2P
209591-67-3P 209591-68-4P 209591-69-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 2-piperazinecarboxamides as inhibitors of MMP or TNF
)

IT 209591-70-8P 209591-71-9P 209591-72-0P
209591-73-1P 209591-74-2P 209591-75-3P
209591-76-4P 209591-77-5P 209591-78-6P
209591-79-7P 209591-80-0P 209591-81-1P
209591-82-2P 209591-83-3P 209591-84-4P
209591-85-5P 209591-86-6P 209591-87-7P
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209592-00-7P 209592-01-8P 209592-02-9P
209592-03-0P 209596-48-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 2-piperazinecarboxamides as inhibitors of MMP or TNF
)

IT 209592-22-3P 209592-23-4P 209593-25-9P
209593-27-1P 209593-28-2P 209593-29-3P
209593-30-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of 2-piperazinecarboxamides as inhibitors of MMP or TNF
)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:761730 CAPLUS
DN 126:31373

TI Preparation of arylsulfonylhydroxamic acid derivatives as matrix metalloproteinase and tumor necrosis factor inhibitors.
IN Piscopio, Anthony D.; Rizzi, James P.
PA Pfizer Inc., USA; Piscopio, Anthony D.; Rizzi, James p.
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9633172	A1	19961024	WO 1995-IB279	19950420
	W: CA, FI, JP, MX, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2218503	AA	19961024	CA 1995-2218503	19950420
	CA 2218503	C	20010724		
	EP 821671	A1	19980204	EP 1995-914486	19950420
	EP 821671	B1	20001227		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
	JP 3053222	B2	20000619	JP 1996-531575	19950420
	JP 10507466	T2	19980721		
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	EP 1995-914486	A	19950420		
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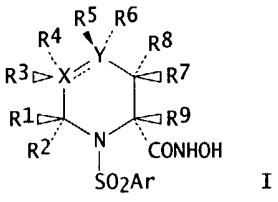

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AB Title compds. [I; X = C, O, S; Y = C, O, S, SO, SO2, N; dotted line = optional double bond; R1-R9 = H, (substituted) alkyl, (CH2)nCOZ; n = 0-6; Z = OH, alkoxy, amino; Ar = (substituted) aryl, heteroaryl; with provisos], were prepd. as drugs (no data). Thus, 1-(4-methoxybenzenesulfonyl)-5-oxopiperazine-2-carboxylic acid (prepn. given) was stirred overnight with O-benzylhydroxylamine, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride, and Et3N in CH2Cl2

to give N-benzyloxy 1-(4-methoxybenzenesulfonyl)-5-oxopiperazine-2-carboxamide, which was hydrogenated to give N-hydroxy 1-(4-methoxybenzenesulfonyl)-5-oxopiperazine-2-carboxamide.

IT **184349-79-9P 184349-80-2P 184349-81-3P**
184349-85-7P 184349-86-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of arylsulfonylhydroxamic acid derivs. as matrix metalloproteinase and tumor necrosis factor inhibitors)

IT **184350-12-7P 184350-21-8P 184350-23-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of arylsulfonylhydroxamic acid derivs. as matrix metalloproteinase and tumor necrosis factor inhibitors)